

Appl. No. : 09/539,032
Filed : March 30, 2000

REMARKS

Claims 1-4 and 6-9 are pending in the present application. Reconsideration and withdrawal of the present rejection in view of the comments presented herein are respectfully requested.

Rejection Under 35 U.S.C. §102(b)

The rejection of Claims 1-4 and 6-9 under 35 U.S.C. §102(b) as allegedly being anticipated by Bruccoleri et al (*Nucl. Acids Res.* 26:4482-2286, 1998) was maintained. The Examiner contends that Bruccoleri et al. teach all of the limitations of Claim 1 (generation of overlapping sequence alignments from pathogenic organisms; homolog matching; target sequence alignment for all sequences; alignment of just matching gene product against the corresponding gene product in the target; and exclusion criteria).

The present invention relates to a method of identifying conserved peptide sequences useful as drug targets by comparing genomes of various pathogenic organisms at the peptide level. This method comprises the following steps as recited in present claim 1:

- i) computationally generating overlapping peptide sequences from selected pathogenic organisms of length 'N',
- ii) computationally sorting the peptide sequences of length 'N' according to amino acid sequence,
- iii) computationally matching the sorted peptide sequences of length 'N' of the selected pathogenic organisms to produce matched common peptide sequences,
- iv) computationally locating the matched common peptide sequences in their corresponding protein sequences to provide locations of said matched common peptide sequences and subsequently labeling the matched common peptide sequences with their origin and location;
- v) computationally joining overlapping common peptide sequences to obtain extended conserved peptide sequences;
- vi) comparing said extended conserved peptide sequences obtained in step (v) to host organism protein sequences to determine which of said conserved peptide sequences from said selected pathogenic organisms are not present in host proteins; and
- vii) communicating said conserved peptide sequences from said selected pathogenic organisms not present in said host proteins to a user.

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In summary, the presently claimed invention relates to the generation of overlapping peptide sequences of length 'N' from selected pathogenic organisms, and comparing these peptides to host organism protein sequences to determine which of these conserved sequences are not present in host proteins. This results in identification of exactly matched conserved peptides.

In contrast to the present claims, the method of Bruccoleri relates to the alignment of sets of selected proteins using FASTA and CLUSTALW programs for identification of conserved regions across various proteins. This method uses BLOSSOM and PAM scoring matrices to identify approximate matches of conserved protein regions. One of ordinary skill in the art would appreciate that comparison of proteins by "Global alignment" as used in FASTA, and as disclosed by Bruccoleri, is not the same as comparison of proteins using peptide blocks as recited in the present claims, nor does the method of Bruccoleri result in exactly matched conserved peptide sequences. The computational tool of Bruccoleri et al. for determining the concordance of putative gene products does not contain all of the features of present claim 1. Bruccoleri does not disclose matching of sorted peptides to produce matched common peptide sequences from selected pathogenic organisms, nor does this reference teach computationally locating matched common peptides in the protein sequence and labeling these matched peptides with their origin and location. In addition, the cited reference does not teach joining of overlapping sequences to obtain extended conserved peptide sequences.

Regarding claims 3 and 4, there is no similarity in the methods of identification of conserved targets described in the cited reference and the presently claimed invention. Sequence ID NO:67 is a stretch of specific conserved peptide sequence located in DNA gyrase, while Bruccoleri has predicted a conserved region of DNA gyrase but has not reported any specific sequence which matches SEQ ID NO:67. The mention of DNA gyrase by the cited reference does not inherently constitute that this sequence is a subunit of DNA gyrase, which itself is a protein of MW 92 KDa, while SEQ ID NO:67 is a small conserved peptide of 10 amino acid residues identified by the presently claimed method.

Thus, none of the steps recited in claim 1, all of which recite manipulations of peptide sequences, are disclosed by this reference. Thus, the claims cannot be anticipated.

In addition, the present claims are not rendered obvious by this reference since the present method unexpectedly results in a much more rapid sequence comparison. For example, the

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comparison of ten proteins, each having 100 amino acids, using the method of Bruccoleri, would require 10^{100} comparisons, while the presently claimed method, if 'N' is 8 , would require only $920 \times 8^2 = \sim 64000$ comparisons. In addition, the presently claimed method does not require pre-classification of proteins which is a pre-requisite of the method of Bruccoleri et al.

In view of the comments presented above, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b).

CONCLUSION

Applicants submit that all claims are in condition for allowance. If any issues remain that could be resolved by telephone, the Examiner is cordially invited to contact the undersigned at the telephone number provided below. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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